October 4, 1954

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My dear Klein:

Thank you for your letter of September 24, answering my questions on Lettre's work. My own reading of this had left me far from convinced and your added comments make it clear that the decisive experiments remain to be done. I would hope that you might find the occasion to go over some of his more pertinent experiments yourself, in addition to the incidental tests of mitotic stimulation. On page 2 you mentioned something about effects of "mitochondria from non-specific sources". I had looked specifically for this experiment in his papers, but did not notice it. Can you direct me to it? I also had the impression that his "nuclear" fractions were relatively inactive, except that fragments did stimulate mitosis. Perhaps these points are taken up in paper IX of his series, which I have not yet seen.

I was particularly interested to hear of your experiments dealing with the possibility of transduction. If you are using as markers, traits that are occasionally subject to spontaneous change, you should have a well-defined system for detecting transduction. And with the ascites, you have an unexampled opportunity to verify the precision of your detection methods by means of reconstruction experiments. This point, the verified possibility of detecting single transformed cells is, of course, the bugaboo of most experiments along these lines. I am sorry I cannot suggest possible examples of transduction in higher organisms— I had hoped to be able to look to you for them eventually. The only things that come anywhere near are in the Medawar-Billingham studies on pigmentation [and I must say I am still not <u>absolutely</u> convinced that the migratory agent is a particle rather than an intact cell], and, at least in hope, some of Mazia's and Brachet-Shaver's on the modification of development in frog eggs by DNA and granules respectively.

The only suggestions I could make would be a) to substantiate the detection procedures by reconstructed mixtures and b) to examine, possibly, a further range of markers— drug resistance (Law) might work very well also. I would also repeat an earlier remark that there is still some mystery about the Stasney et al. story, if intact cells ahev not been directly demonstrated. How about the effect of DNAase in that system?

Of course I am happy to continue to exchange papers with you. Lately I've been too busy with the micromanipulation of conjugal pairs to keep up with my office chores.

Yours sincerely,

P.S. Have you the markers that would enable you to pick up, selectively, recombination between intact cells in "mixed culture"?

Joshua Lederberg